

NONINVASIVE pH-TELEMETRIC MEASUREMENT OF
GASTROINTESTINAL FUNCTION

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ABSTRACT

The purpose of this study was to gain experience with and validate the Heidelberg pH-telemetric methodology in order to determine if the pH-telemetric methodology would be a useful noninvasive measure of gastrointestinal transit time for future ground-based and in-flight drug evaluation studies. The Heidelberg pH metering system is a noninvasive, nonradioactive telemetric system that, following oral ingestion, continuously measures intraluminal pH of the stomach, duodenum, small bowel, ileocecal junction, and large bowel. Gastrointestinal motility profiles were obtained in normal volunteers using the lactulose breath-hydrogen and Heidelberg pH metering techniques. All profiles were obtained in the morning after an overnight fast. Heidelberg pH profiles were obtained in the fasting and fed states; lactulose breath-hydrogen profiles were obtained after a standard breakfast. Mouth-to-cecum transit time was measured as the interval from administration of lactulose (30 ml; 20 g) to a sustained increase in breath hydrogen of 10 ppm or more. Gastric emptying time was measured as the interval from the administration of the Heidelberg capsule to a sustained increase in pH of 3 units or more. Technical problems limited the number of gastric motility profiles obtained. However, mouth-to-cecum transit time, peak hydrogen, and time to peak hydrogen as measured by the lactulose breath-hydrogen test did not appear to be changed by the co-administration of the Heidelberg capsule. Food prolonged gastric emptying of the Heidelberg capsule. It appears that each method assesses a different component of the gastrointestinal system. These two methodologies test distinctly different components of gastrointestinal motility and together may provide a more complete assessment of gastrointestinal motility.

INTRODUCTION

One of NASA's scientific goals is to describe and understand human adaptation to the space environment and to use this knowledge to improve the health, safety, and performance of the astronauts (1). The absorption of orally administered drugs depends on characteristics of the drug (solubility, ionization, etc.), the nature of the formulation (solution, suspension, tablet, etc.) and the physiology of the gastrointestinal tract (pH, surface area, blood flow, etc.). Gastrointestinal hypokinesia associated with bed rest results in decreased appetite, indigestion, and constipation. Preliminary observations suggest that the microgravity also may cause gastrointestinal hypokinesia. Because gastrointestinal absorption of medications and nutrients depends on gastrointestinal pH, motility, and splanchnic blood flow, it is necessary to characterize how these parameters are altered by microgravity in order to develop appropriate countermeasures. The purpose of this study was to gain experience with the Heidelberg pH-telemetric system in order to determine if the pH-telemetric methodology would be a useful noninvasive measure of gastrointestinal transit time for future ground-based and in-flight drug development and assessment studies.

BACKGROUND

Gastrointestinal Physiology

Each organ of the gastrointestinal tract (esophagus, stomach, small intestine, large intestine) is anatomically and physiologically distinct. The proximal stomach stores food; the antrum grinds and sieves food. Liquids are emptied from the stomach by a rapid first-order phase followed by a slower first-order phase. This is in contrast to gastric emptying of solids, which tends to be more sigmoid in nature. For solids, there is an initial long lag phase which is followed by a prolonged linear phase, and finally, when the stomach is nearly empty, by a very slow zero-order phase. Gastric emptying of large, indigestible particles is thought to occur during the phase III contractions of the interdigestive myoelectric motility waves ("housekeeping waves") that occur every 90-120 minutes. It is not known whether microgravity-induced changes in gastrointestinal motility affect each organ to the same extent or if different organs are affected to different degrees.

The Heidelberg pH Meter Test

The Heidelberg pH metering system is a noninvasive, nonradioactive telemetric system that, following oral ingestion, continuously measures intraluminal gastrointestinal pH. The system consists of the pH metering

capsule, a belt antenna, a receiving console, and a heating module. The capsule is approximately the size of a No. 1 gelatin capsule (7 x 20 mm) and has a density of 1.5 g/cm³. The capsules are not sterilizable and are intended for one application.

The Heidelberg pH metering system was originally marketed as a noninvasive diagnostic tool for the evaluation of various hypo- and hypersecretory acid states and motility disorders. More recently, the Heidelberg pH metering system has been used to evaluate the effect of a variety of parameters such as food (2), gender, posture, and age on gastric residence time (3). The system has also been used to evaluate the effect of gastric residence time on the absorption of enteric-coated aspirin (4-5) and procainamide (6) as well as the effect of drugs such as ranitidine (7), omeprazole (8), loperamide, and metoclopramide (9) on various components of gastrointestinal transit time.

The Heidelberg pH-telemetric system measures the intraluminal pH of the stomach, duodenum, small bowel, ileocecal junction, and large bowel. In addition to measuring the pH of different segments of the gastrointestinal tract, the gastric emptying time, can be determined from the characteristic pH-time profile. Gastric emptying time is the interval from the ingestion of the capsule to a sharp, sustained increase in pH of 3 units or more. The accurate measuring range is H 1.0 to 8.0 with a measuring error of +/- 0.5pH units (10).

Typical parameters for young male normal volunteers after standard feeding include a gastric residence time of 3.5 +/- 0.6 hours, duodenal pH of 5.8 +/- 0.8, small bowel transit time of 2.8 to > 5 hours, and mouth to cecum transit time within 9 hours (11). Gastric residence time appears to be reproducible (no difference between parameters when taken at one week intervals) and postural changes (supine flat on the back versus standing) do not appear to alter gastric residence time (11). However, gastric residence time is prolonged with increasing age and in females even when hormonal changes due to the menstrual cycle are normalized.

STUDY DESIGN

Gastrointestinal motility profiles were obtained in normal volunteers using the lactulose breath-hydrogen and Heidelberg pH metering techniques. All profiles were obtained in the morning after an overnight fast and/or a standard breakfast. The standard breakfast consisted of a hard boiled egg, two slices of bread/toast lightly buttered, 4 oz. orange juice, and a cup of decaffeinated coffee or tea. The breakfast was consumed within a 15 minute interval; the orange juice was consumed at the end of the meal with the test material. Lactulose breath-hydrogen was measured

before and every 10 minutes for 4 hours after the lactulose was consumed. End-alveolar breath was collected and analyzed for hydrogen content. Mouth-to-cecum transit time was measured as the interval from administration of the lactulose (30 ml; 20 g) to a sustained increase in breath hydrogen of 10 ppm or more. Gastric emptying time was measured as the interval from the administration of the Heidelberg capsule to the time when there was a sustained increase in pH of 3 units or more.

RESULTS

Gastrointestinal Profiles

Technical problems limited the number of gastrointestinal motility profiles obtained. However, some trends are evident. The mouth-to-cecum transit time, peak hydrogen, and time to peak hydrogen as measured by the lactulose breath-hydrogen test did not appear to change when lactulose was administered alone or co-administered with the Heidelberg capsule (the values ranged from 60-90 min. vs. 80 min.; 40-97 ppm vs. 56 ppm; and 30-90 vs. 50 min., respectively). Food prolonged gastric emptying of the Heidelberg capsule (320 min. fed vs. 30-38 min. fasting).

Procedures

Appropriate functioning of the Heidelberg pH-telemetric system depends on close attention to operational details. The following additions to the procedures supplied in the manual are recommended:

1. Turn the heating module on at least one hour prior to administration of the capsule. Set the left hand knob to 3.5. The module is very slow to reach equilibrium and very sensitive to the setting. Do not try to rush the warm-up period by setting the knob higher than 3.5.
2. Fill the stainless steel rinse dish to within one-half inch of the rim with deionized water. Do not use tap water. Replace the rinse water if more than two or three calibration checks are necessary.
3. Fill a 16 x 100 mm disposable glass culture tube one-half full with 0.9% sodium chloride. It is absolutely necessary to have in-date and accurately prepared 0.9% sodium chloride solutions. Do not try to make the 0.9% sodium chloride from laboratory or table sodium chloride. Non-preserved, single use injectable 0.9% sodium chloride solutions work well with the system, but do not save the bottle or bag for another test.

4. Using long-nose forceps, gently place the capsule, white end up, into the tube with the 0.9% sodium chloride. Observe two or three bubbles leave the capsule and then gently scrape the white mesh of the capsule with a fingernail to break the surface tension. It is absolutely essential that the white mesh is saturated with solution and not covered with air. Leave the capsule undisturbed for at least 15-20 minutes. (Disregard the company's recommendation of a 2 minute soaking interval).

Problem Shooting. All capsules can be calibrated. If the capsule calibrates to pH 1 initially, but will not calibrate to pH 7, the 0.9% sodium chloride is at fault. Change to a different lot or brand of 0.9% sodium chloride and start over with another capsule. Soak the the original capsule in deionized water for 20-30 minutes and dry at room temperature for at least 48 hours before attempting to recalibrate with new 0.9% sodium chloride. If the capsule will not calibrate to pH 1, there is something wrong with the system. The problem may be with the calibration antenna, which is the most sensitive component of the system. Unplug the calibration antenna from the console and take the acrylic block out of the heater module and place it on the center of the antenna belt. This allows the capsule to be calibrated with the antenna belt directly and bypasses the calibration antenna. Calibrate the capsule as above. If this fails, contact the company for further advice.

RECOMMENDATIONS

The Heidelberg pH-telemetric system is a relatively simple, noninvasive method for the assessment of the gastric emptying rate. Although the calibration of the system is a little tricky and very dependent on the accuracy of the 0.9% sodium chloride, the noninvasiveness of the test and the lack of dependency on the degree of subject cooperation make it a good evaluation method for in-flight testing. It is not clear whether the gastric emptying rate of the large indigestible capsule reflects true gastric emptying of food particles or just the final housekeeping phase of gastric emptying.

The exact relationship between changes in gastrointestinal motility as measured by the lactulose breath-hydrogen method and the Heidelberg pH-telemetric method remains to be determined. From the limited data obtained in this study, it appears that each method assesses a different component of the gastrointestinal system. Measurement of gastrointestinal function with both of these methodologies may provide a more complete view of gastrointestinal function. The influence of one test material on the other has yet to be determined, but it appears that each test functions independently of the other.

Several equipment changes are recommended before the system is considered for in-flight studies. A small, hand-sized console unit should be developed that could be clipped to a belt. This would allow the astronaut to be completely mobile throughout the testing period. Another alternative would be to develop a hand-sized recorder that would receive and record the battery signals. A final concern is with the size of the calibration capsule. Emptying of a smaller sized capsule may be a more accurate measure of gastric emptying of food particles and a more realistic evaluation of gastric function.

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